# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

SM

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/032,393 | 12/21/2001 | Robert Haselbeck | ELITRA.010A | 5173 |

20995 7590 02/25/2004

KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

| EXAMINER |
|---|
| VOGEL, NANCY S |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1636 | |

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/032,393 | HASELBECK ET AL. | |
| | Examiner | Art Unit | |
| | Nancy Vogel | 1636 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-135* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-135* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-47, drawn to a nucleic acid comprising a fusion promoter comprising at least one promoter that is modified to have altered activity in at least one gram-positive organism, linked to at least one operator, vectors comprising said nucleic acid, and host cells comprising said nucleic acid, classified in class 536, subclass 24.1, class 435, subclasses 320.1 and 252.3, 25231, 252.35.

II. Claims 48-62, drawn to a method for identifying genes involved in cellular proliferation by identifying cells in a cell population whose proliferation is reduced in response to induction of transcription of a nucleic acid, classified in class 435, subclass 6.

III. Claims 63-77, drawn to a method for identifying genes involved in cellular proliferation by comparing the proliferation of a cell cultured in the presence of a first concentration of an inducer to that of a cell cultured in the presence of a second concentration of the inducer, classified in class 435, subclass 6.

IV. Claims 78-89, drawn to a method for identifying a compound which reduces the activity or level of a gene product required for proliferation of a

cell, and said compound, classified in class 435, subclass 6, and unclassifiable (compound claim)

V. Claims 90-100, drawn to a method of inhibiting the activity or expression of a gene in an operon required for proliferation, classified in class 435, subclass 471.

VI. Claims 101-111, drawn to a method of manufacturing an antibiotic, classified in class 435, subclass 69.1.

VII. Claims 112-117, drawn to a method for identifying a gene required for proliferation of a prokaryotic cell by identifying cells in which the extent of proliferation of said cell when a fusion promoter is active at a first level is substantially different than the extent of proliferation of said cell when said fusion promoter is active at a second level, classified in class 435, subclasses 6 and 455.

VIII. Claims 118-122, drawn to a method for identifying a compound which inhibits the proliferation of a prokaryotic cell comprising replacing the native promoter of a gene, classified in class 435, subclass 32 and 455.

IX Claims 123-126, drawn to a method for identifying a gene which is required for proliferation of a prokaryotic cell, classified in class 435, subclass 32.

X. Claims 127-130, drawn to a method of identifying a compound which inhibits the proliferation of a prokaryotic cell comprising obtaining a prokaryotic cell in which transcription of a nucleic acid required for

proliferation is regulated by at least one operator which has been introduced into the chromosome of said cell, classified in class 435, subclass

XI. Claims 131-135, drawn to a method of identifying a nucleic acid sequence having promoter activity in Enterococcus faecalis, classified in class 435, subclass 6.

The inventions are distinct, each from the other because of the following reasons:

Inventions of Group I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claimed can be used in a different process, such as in a method of in vitro hybridization, wherein the nucleic acid product is used as a probe.

Inventions of Group I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claimed can be used in a different method, such as an in vitro method of hybridization, wherein the nucleic acid product is used as a probe.

Inventions of Group I and IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claimed can be used in a different method, such as an in vitro method of hybridization, wherein the nucleic acid product is used as a probe.

Inventions of Group I and V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claimed can be used in a different method, such as an in vitro method of hybridization, wherein the nucleic acid product is used as a probe.

Inventions of Group I and VI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claimed can be used in a different method, such as an in vitro method of hybridization, wherein the nucleic acid product is used as a probe.

Inventions of Group I and VII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claimed can be used in a different method, such as an in vitro method of hybridization, wherein the nucleic acid product is used as a probe.

Inventions of Group I and VIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claims can be used in a different method, such as an in vitro method of hybridization, wherein the nucleic acid product is used as a probe.

The inventions of Group I and Groups IX-XI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP 806.04, MPEP 808.01). In the instant case the products of Group I are not used in or made by the method of Groups IX-XI.

Inventions of Groups II-XI are biologically and functionally different and distinct from each other and thus one does not render the other obvious. The methods of Groups II-XI comprise steps which are not required for or present in the methods of the

other groups: inducing transcription of a nucleic acid from the inducible promoter (Group II); comparing proliferation of a cell cultured in the presence of a first concentration of an inducer with proliferation in the presence of a concentration of inducer that is less than said first concentration (Group III); sensitizing the cell by inducing transcription from the fusion promoter, contacting said sensitized cell with a compound and determining the degree to which a compound inhibits proliferation of the sensitized cell relative to a cell which has not been sensitized (Group IV); introducing into a cell a construct comprising an inducible fusion promoter operably linked to a nucleic acid that is complementary to at least a portion of a proliferation-required operon (Group V); manufacturing a compound which inhibits the proliferation of a cell (Group VI); replacing the native promoter of a gene in the chromosome of a prokaryotic cell having an enhanced frequency of homologous recombination (Group VII); comparing the extent of proliferation of a first sample of a cell in the presence of a compound to the extent of proliferation of a second sample of said cell in the presence of said compound (Group VIII); introducing at least one operator into a prokaryotic cell (Group IX); obtaining a prokaryotic cell in which transcription of a nucleic acid required for proliferation of said cell is regulated by a least one operator which has been introduced in the chromosome (Group X); and introducing a candidate nucleic acid into a vector comprising lacL-lacM reporter genes (Group XI) . The end result of the methods are different: identification of genes involved in cellular proliferation (the different method steps would result in different genes being identified) (Groups II, III, VII); identification of a compound which reduces the activity or level of a gene product required for

proliferation of a cell (Group IV); inhibition of the activity or expression of a gene in an operon required for proliferation (Group V); production of an antibiotic (Group VI); identification of a gene required for proliferation of a prokaryotic cell (Group VII and IX); identification of a compound which inhibits proliferation of a prokaryotic cell (Group VIII and X); and identification of a nucleic acid having promoter activity in Enterococcus faecalis (Group XI) . Thus, the operation, function and effects of these different methods are different and distinct from each other. Therefore, the inventions of these different, distinct groups are capable of supporting separate patents.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper. Further more, especially in instances where the classifications are the same, the non-patent literature searches required for each of these inventions are not co-extensive, hence said searches would be burdensome. Therefore, restriction for examination purposes as indicated is proper.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final

rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim

remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

This application contains claims directed to the following patentably distinct species of the claimed invention:

Regarding Groups I-VIII, a nucleic acid, a method of identifying genes involved in cell proliferation using said nucleic acid, a method of identifying compounds that reduce activity of a gene product required for proliferation using said nucleic acid, method of inhibiting activity or expression of a gene in an operon required for proliferation using said nucleic acid, method of manufacturing an antibiotic using said nucleic acid, method of identifying a gene required for proliferation of a prokaryotic cell using said nucleic acid, method for identifying a compound which inhibits the proliferation of a prokaryotic cell using said nucleic acid, wherein said nucleic acid is: a fusion promoter comprising at least one promoter that is modified to have altered activity in at least one gram-positive organism, said promoter being linked to at least one operator, wherein the promoter is selected from SEQ ID NOs: 36-45 , the operator is selected from xylO, tetO, trpO, malO, and lambdac1O, and wherein the gram positive organism is selected from B. anthracis, C. botulinum, C. difficil, C. perfringens, C. teteni, C. diptheriae, E. faecalis, E. faecium, L. lactis, L. monosytogenes, M. leprae, M. tuberculosis, N. asteroids. S. aureus, S. epidermis, S. xylosis, S. pneumoniae, S. mutans.

Regarding Group IX and X, a method for identifying a gene which is required for proliferation of a prokaryotic cell, or a method of identifying a compound which inhibits the proliferation of a prokaryotic cell, each utilizing an operator selected from xylO, tetO, trpO, malO, lacO and lambdac1O.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. One promoter fusion comprising one promoter and one operator, and one gram positive organism should be elected if any of Groups I- VIII are elected. Currently, claims 1, 48, 78, 90, 101, 112, 118 are generic. One operator sequence should be elected if either of Groups IX or X are elected.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record

showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 6:30 - 3:00, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3014.

ntv

TERRY MCKELVEY
PRIMARY EXAMINER